

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A vaccine composition comprising an isolated protein belonging to the Bcl-2 protein family or an immunogenically active peptide fragment hereof or a nucleic acid encoding said protein or said peptide fragment for use as a medicament.

2. (Original) The composition of claim 1, wherein the vaccine composition when administered to a cancer patient, is capable of eliciting an immune response against the cancer disease.

3. (Currently Amended) The composition of claim 1, wherein the vaccine composition, when administered to a cancer patient where a Bcl-2 protein family member is expressed, is capable of eliciting an immune response against the cancer disease.

4. (Currently Amended) The vaccine composition according to ~~any of claims~~ claim 1 to 3, wherein the protein is selected from the group consisting of anti-apoptotic members of the Bcl-2 family.

5. (Currently Amended) The vaccine composition according to ~~any of claims~~ claim 1 to 3, wherein the protein is selected from the group consisting of Bcl-2, Bcl-w, Mcl-1, Bfl-1/A1, Bcl-b, Bcl2-L-10 and Bcl-X_L.

6. (Currently Amended) The vaccine composition according to ~~any of claims~~ claim 1 to 3, wherein the protein is selected from the group consisting of Bax, Bok/Mtd, Bad, Bik/Nbk, Bid, Hrk/DP5, Bim, Noxa, Bmf and PUMA/bbc3.

7. (Original) The vaccine composition of claim 5, wherein the protein is Bcl-2.

8. (Currently Amended) The vaccine composition of claim 5, wherein the protein is Bcl-X_L.

9. (Currently Amended) The vaccine composition according to claim 5, wherein the protein is Mcl-1.

10. (Currently Amended) An isolated immunogenically active peptide fragment derived from a protein belonging to the Bcl-2 protein family, ~~for use and useful~~ as a medicament in the prevention or treatment of a cancer.

11. (Original) The peptide fragment according to claim 10, wherein the protein is selected from the group consisting of Bcl-2, Bcl-w, Mcl-1, Bfl-1/A1, Bcl-b, Bcl2-L-10 and Bcl-X_L.

12. (Original) The peptide fragment according to claim 10, wherein the protein is selected from the group consisting of Bax, Bok/Mtd, Bad, Bik/Nbk, Bid, Hrk/DP5, Bim, Noxa, Bmf and PUMA/bbc3.

13. (Currently Amended) The peptide fragment according to claim 11, wherein the protein is Bcl-2.

14. (Currently Amended) The peptide fragment according to claim 11, wherein the protein is Bcl-X_L.

15. (Currently Amended) The peptide fragment according to claim 11, wherein the protein is Mcl-1.

16. (Currently Amended) The peptide fragment according to ~~any of claims~~ claim 10 to 15 that is capable of eliciting a cellular immune response in a cancer patient.

17. (Currently Amended) The peptide fragment according to ~~any of claims~~ claim 10 to 16, which is an MHC Class I-restricted peptide having at least one of the following characteristics:

(i) capable of binding to the Class I HLA molecule to which it is restricted at an affinity as measured by the amount of the peptide that is capable of half maximal recovery of the Class I HLA molecule (C₅₀ value) which is at the most 50 μ M as determined by the assembly binding assay as described herein,

(ii) capable of eliciting INF- γ -producing cells in a PBL population of a cancer patient at a frequency of at least 1 per 10⁴ PBLs as determined by an ELISPOT assay, and/or

(iii) capable of *in situ* detection in a tumor tissue of CTLs that are reactive with the epitope peptide.

18. (Original) The peptide fragment of claim 17 having a C_{50} value, which is at the most 30 μ M.

19. (Original) The peptide fragment of claim 17 having a C_{50} value, which is at the most 20 μ M.

20. (Original) The peptide fragment of claim 17, which is restricted by a MHC Class I HLA-A molecule.

21. (Original) The peptide fragment of claim 20, which is restricted by a MHC Class I HLA species selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11 and HLA-A24.

22. (Original) The peptide fragment of claim 17, which is restricted by HLA-A2.

23. (Currently Amended) The peptide fragment according to ~~any of claims claim 10 to 11 and 16 to 19~~, which comprises a sequence selected from the group consisting of ALVGACITL (SEQ ID NO:1), ALSPVPPVV (SEQ ID NO:2), SLALVGACI (SEQ ID NO:3), KTLTSLALV (SEQ ID NO:4), LLSLALVGA (SEQ ID NO:5), WLSLKTLLSL (SEQ ID NO:6), AAAGPALSPV (SEQ ID NO:7), PLFDFSWLSL (SEQ ID NO:8), FTARGRFATV (SEQ ID NO:9), YLNRHLHTWI (SEQ ID NO:10), and NIALWMTEYL (SEQ ID NO:11).

24. (Currently Amended) The peptide fragment according to ~~any of claims claim 10 to 11 and 16 to 19~~, wherein the peptide comprises a sequence selected from the group consisting of TAYQSFEQV (SEQ ID NO:43), YLNDHLEPWI (SEQ ID NO: 42), RIAAWMATYL

(SEQ ID NO:45), WMATYLNDHL (SEQ ID NO:46), VLVSRIAAWM (SEQ ID NO: 48) and VAFFSFGGAL (SEQ ID NO: 49),.

25. (Currently Amended) The peptide fragment according to ~~any of claims claim 10 to 11 and 16 to 19~~, wherein the peptide comprises the sequence RIAAWMATY (SEQ ID NO:50).

26. (Currently Amended) The peptide fragment according to ~~any of claims claim 10 to 11 and 16 to 19~~, wherein the peptide comprises a sequence selected from the group consisting of RLLFFAPTR (SEQ ID NO:55) and RTKRDWLVK (SEQ ID NO:56).

27. (Currently Amended) The peptide fragment according to ~~any of claims claim 10 to 11 and 16 to 19~~, wherein the peptide comprises a sequence selected from the group consisting of PAEEEEDDL Y (SEQ ID NO:58) and QSLEIISRY (SEQ ID NO:60).

28. (Currently Amended) The peptide fragment according to ~~any of claims claim 10 to 11 and 16 to 19~~, wherein the peptide is selected from the group consisting of RLKRDWLVK (SEQ ID NO:62), QSDEIISRY (SEQ ID NO:63) and QSEEIISRY (SEQ ID NO:64).

29. (Original) The peptide fragment of claim 17, which is restricted by a MHC Class I HLA-B molecule.

30. (Original) The peptide fragment of claim 29, which is restricted by a MHC Class I HLA-B species selected from the group consisting of HLA-B7, HLA -B35, HLA -B44, HLA-B8, HLA-B15, HLA-B27 and HLA-B51.

31. (Currently Amended) The peptide fragment according to ~~any of claims~~
claim 10 to 30 comprising at the most 20 amino acid residues.

32. (Original) The peptide fragment of claim 31 comprising at the most 15
amino acid residues.

33. (Original) The peptide fragment of claim 32, which is a nonapeptide or a
decapeptide.

34. (Currently Amended) The protein or peptide fragment according to ~~any of~~
~~claims-~~ claim 10 to 33, which is a native sequence isolated or derived from a mammal species.

35. (Currently Amended) The protein or peptide fragment according to ~~any of~~
~~claims-~~ claim 10 to 34 where the protein is a human protein.

36. (Currently Amended) The protein or peptide fragment according to ~~any of~~
~~claims-~~ claim 10 to 33, which is derived from a native Bcl-2 protein family member sequence by
substituting, deleting or adding at least one amino acid residue.

37. (Currently Amended) The peptide fragment according to ~~any of claims~~
claim 10 to 36 comprising, for each specific HLA allele, any of the amino acid residues as
indicated in the following table:

HLA al- lele	Position 1	Position 2	Position 3	Position 5	Position 6	Position 7	C-termi- nal
HLA-A1		T,S	D,E			L	Y

HLA-A2		L, M			V	L, V
HLA-A3		L, V, M	F, Y			K, Y, F
HLA-A11		V, I, F, Y	M, L, F, Y, I			K, R
HLA-A23		I, Y				W, I
HLA-A24		Y		I, V	F	I, L, F
HLA-A25		M, A, T	I			W
HLA-A26	E, D	V, T, I, L, F			I, L, V	Y, F
HLA-A28	E, D	V, A, L				A, R
HLA-A29		E				Y, L
HLA-A30		Y, L, F, V				Y
HLA-A31			L, M, F, Y			R
HLA-A32		I, L				W
HLA-A33		Y, I, L, V				R
HLA-A34		V, L				R
HLA-A66	E, D	T, V				R, K
HLA-A68	E, D	T, V				R, K
HLA-A69		V, T, A				V, L
HLA-A74		T				V, L

HLA-B5		A,P	F,Y			I,L
HLA-B7	R,A	P				L,F
HLA-B8			K	K,R		L
HLA-B14		R,K				L,V
HLA-B15		Q,L,K,P,				F,Y,W
(B62)		H,V,I,M,				
HLA-B17		S,T				L,V
HLA-B27		R				Y, K,F,L
HLA-B35		P				I, L, M, Y
HLA-B37		D,E				I,L,M
HLA-B38		H	D,E			F,L
HLA-B39		R,H				L,F
HLA-B40		E	F,I,V			L,V,A,W,
(B60,61)						M,T,R
HLA-B42		L,P				Y,L
HLA-B44		E				F,Y,W
HLA-B46		M,I,L,V				Y,F
HLA-B48		Q,K				L
HLA-B51		A,P,G				F,Y,I,V
HLA-		Q	F,Y			I,V

B52							
HLA-	P					W,F,L	
B53							
HLA-	P						
B54							
HLA-	P					A,V	
B55							
HLA-	P					A,V	
B56							
HLA-	A,T,S					F,W,Y	
B57							
HLA-	A,T,S					F,W,Y	
B58							
HLA-	P					L	
B67							
HLA-	R					P	
B73							
HLA-	A,L					L	
Cw1							
HLA-	A,L					F,Y	
Cw2							
HLA-	A,L					L,M	
Cw3							
HLA-	Y,P,F					L,M,F,Y	
Cw4							
HLA-	Y					L,Y,F,Y	
Cw6							
HLA-	Y					L,I,	
Cw8							
HLA-	A,L					L,V	
Cw16							

38. (Currently Amended) The peptide fragment according to ~~any of claims~~ claim 10 to 37 that is capable of eliciting INF- γ -producing cells in a PBL population of a cancer patient at a frequency of at least 10 per 10^4 PBLs.

39. (Currently Amended) The peptide fragment according to ~~any of claims~~ claim 10 to 38, which is capable of eliciting INF- γ -producing cells in a PBL population of a patient having a cancer disease where a protein belonging to the Bcl-2 protein family is expressed.

40. (Currently Amended) The peptide fragment of claim 39 where the cancer disease is selected from the group consisting of a haematopoietic malignancy ~~including chronic lymphatic leukemia and chronic myeloid leukemia~~, melanoma, breast cancer, cervix cancer, ovary cancer, lung cancer, colon cancer, pancreas cancer and prostate cancer.

41. (Currently Amended) The vaccine composition according to ~~any of claims~~ claim 1 to 9 comprising ~~the~~ a peptide fragment according to any of claims 10 to 40 which is an isolated immunogenically active peptide fragment derived from a protein belonging to the Bcl-2 protein family.

42. (Currently Amended) The vaccine composition of claim 41 wherein said ~~that comprises a peptide fragment according to claim 18 in combination with a peptide fragment according to claim 29~~ has a C_{50} value which is at the most 30 μ M.

43. (Currently Amended) The vaccine composition according to ~~any of claims~~ claim 1 to 9 and 41 to 42 where the vaccine elicits the production in a vaccinated patient of effector T-cells having a cytotoxic effect against the cancer cells.

44. (Currently Amended) The vaccine composition according to ~~any of claims claim 1 to 9 and 41 to 43~~ further comprising an immunogenic protein or peptide fragment selected from a protein or peptide fragment not belonging to or derived from the Bcl-2 protein family.

45. (Original) The vaccine composition of claim 44 where the protein or peptide fragment not belonging to or derived from the Bcl-2 protein family is a protein involved in regulation of cell apoptosis or a peptide fragment derived therefrom.

46. (Currently Amended) The vaccine composition of claim 44 where the immunogenic protein or peptide fragment selected from a protein or peptide fragment not belonging to or derived from the Bcl-2 protein family is survivin or a peptide fragment thereof.

47. (Currently Amended) The vaccine composition of claim 44 where the immunogenic protein or peptide fragment selected from a protein or peptide fragment not belonging to or derived from the Bcl-2 protein family is ML-IAP or a peptide fragment thereof.

48. (Currently Amended) The vaccine composition according to ~~any of claims claim 1 to 9 and 41 to 47~~, wherein the composition comprises an adjuvant.

49. (Original) The vaccine composition according to claim 48, wherein the adjuvant is selected from the group consisting of bacterial DNA based adjuvants, oil/surfactant based adjuvants, viral dsRNA based adjuvants and imidazochinilines.

50. (Currently Amended) The vaccine composition according to ~~any of claims claim 1 to 9 and 41 to 49~~, wherein the vaccine composition comprises antigen presenting cells comprising the protein or peptide fragment or nucleic acid.

51. (Original) The vaccine composition according to claim 50, wherein the antigen presenting cell is a dendritic cell.

52. (Currently Amended) The vaccine composition according to ~~any of claims claim 1 to 9 and 41 to 51~~, wherein the composition comprises a liposome.

53 (Cancelled).

54. (Currently Amended) The vaccine composition according to ~~any of claims claim 1 and 53~~, wherein the nucleic acid is comprised within a vector.

55. (Original) The vaccine composition according to claim 54, wherein the vector is selected from the group consisting of viral vectors and bacterial vectors.

56. (Currently Amended) The vaccine composition according to ~~any of claims claim 54 to 55~~, wherein the vector furthermore comprises nucleic acids encoding a T-cell stimulatory polypeptide.

57. (Original) The vaccine composition according to claim 56, wherein the T-cell stimulatory polypeptide is selected from the group consisting of B7.1, ICAM-1 and LFA-3.

58. (Currently Amended) A kit-of-parts comprising the vaccine composition according to ~~any of claims~~ claim 1 to 9 and 41 to 57, and a further anti-cancer agent.

59. (Currently Amended) The kit-of-parts according to claim 58, wherein the anti-cancer agent is an antibody.

60. (Original) The kit-of-parts according to claim 59, wherein the anti-cancer agent is a cytokine.

61. (Currently Amended)) A composition for *ex vivo* or *in situ* diagnosis of the presence in a cancer patient of T cells in PBL or in tumor tissue that are reactive with a Bcl-2 protein family member, the composition comprising a peptide fragment according to ~~any of claims~~ claim 10 to 40.

62. (Currently Amended) A diagnostic kit for *ex vivo* or *in situ* diagnosis of the presence in a cancer patient of T cells in PBL or in ~~tumour~~ tumor tissue that are reactive with a Bcl-2 protein family member, the kit comprising a peptide fragment according to ~~any of claims~~ claim 10 to 40.

63. (Currently Amended) A complex of a peptide fragment according to ~~any of claims~~ claim 10 to 40 and a Class I HLA molecule or a fragment of such molecule.

64. (Original) The complex of claim 63 which is monomeric.

65. (Original) The complex of claim 63 which is multimeric.

66. (Currently Amended) A method of detecting in a cancer patient the presence of a Bcl-2 protein family member reactive T-cells, the method comprising contacting a ~~tumour~~ tumor tissue or a blood sample with a complex of claim 63 and detecting binding of the complex to the tissue or the blood cells.

67. (Currently Amended) A molecule that is capable of binding specifically to a peptide fragment according to ~~any of claims~~ claim 10 to 40.

68. (Original) The molecule of claim 67 which is an antibody or a fragment hereof.

69. (Original) The molecule according to claim 67, wherein the molecule is a T-cell receptor.

70. (Currently Amended) A molecule that is capable of blocking the binding of the molecule of claim 67 ~~or 69~~.

71. (Currently Amended) A method of treating a cancer disease, the method comprising administering to a patient suffering from the disease an effective amount of the composition according to ~~any of claims~~ claim 1 to 9 and 41 to 57, ~~the molecule of claim 67 or the molecule of claim 70 or the kit of parts according to any of claims 58 to 60.~~

72. (Original) The method of claim 71 wherein the disease to be treated is a cancer disease where a Bcl-2 protein family member is expressed.

73. (Currently Amended) The method of claim 71 wherein the cancer disease is selected from the group consisting of a haematopoietic malignancy ~~including chronic lymphatic leukemia and chronic myeloid leukemia~~, melanoma, breast cancer, cervix cancer, ovary cancer, lung cancer, colon cancer, pancreas cancer and prostate cancer.

74. (Currently Amended) The method of ~~to~~-claim 71, which is combined with a further cancer treatment.

75. (Currently Amended) The method of claim 71 wherein the further treatment is selected from the group consisting of chemotherapy, ~~radiotherapy~~ radiotherapy, treatment with immunostimulating substances, gene therapy, treatment with antibodies and treatment using dendritic cells .

76-80. (Cancelled)

81. (Original) A method of monitoring immunisation, said method comprising the steps of

- i) providing a blood sample from an individual
- ii) providing a protein belonging to the Bcl-2 protein family or a peptide fragment hereof
- iii) determining whether said blood sample comprises antibodies or T-cells comprising T-cell receptors specifically binding the protein or peptide
- iv) thereby determining whether an immune response to said protein or peptide has been raised in said individual.

82. (Currently Amended) The method according to claim 81, wherein ~~the a~~ peptide fragment is ~~a peptide fragment according to any of claims~~ provided.

83. (Original) An isolated T-cell comprising a T-cell receptor according to claim 69.